

REMARKS

Claims 1, 5, 8-10, 12 and 15-37 are pending in this case and stand rejected in a non-final Office Action mailed May16, 2008. Claims 15-31 have been withdrawn from consideration in view of a restriction requirement.

Herein Applicants are canceling claims 1, 5, 8-10 and 12 without prejudice, amending claims 32, 36 and 37, and adding new independent claim 38 and dependent claim 39. In view of the claim amendments and Applicants remarks, Applicants respectfully request the Examiner's consideration and allowance of claims 32-39.

Applicants thank the Examiner for withdrawing the final status of the previous office action in view of Applicants' request for continued examination. Additionally Applicants thank the Examiner for withdrawing the rejections of claim 1 under 35 U.S.C. 112 1st paragraph, claims 1-4,5,7-9 and 14 under 35 USC 102 (b) over Mizumoto et al. and Claims 1,4,5, 7-9 and 14 under 35 U.S.C. 102(e) over Shimizu.

Amended Claims

Amended independent claim 32 is presented for the Examiner's consideration. Applicants have included the additional limitations of "a single saccharide" and the limitation that the fast dissolve granulation consists essentially of a "portion of single" saccharide. This amendment is supported, for example, by Example 8 of the specification. The Applicants have also amended claim 32 to recite "a hardness of less than about 1.7 kP". Support for this amendment is found in Example 8, for example. As claims 33-36 variously depend from claim 32, the amendment likewise applies to dependent claims 33-35 that depend from claim 32.

Amended independent claim 36 is presented for the Examiner's consideration. Applicants have included the additional limitations of "a single saccharide", and the limitation that the fast dissolve granulation consists essentially of a "portion of the single" saccharide. This amendment is supported, for example, by Example 8 of the specification. The Applicants have also amended claim 32 to recite "a hardness of less than about 1.7 kP". Support for this amendment is found in Example 8, for example. These amendments likewise apply to claim 37 which has been amended to depend from claim 36.

Applicants believe that these amended claims further point out and distinguish Applicants' invention. Applicants respectfully request that the Examiner consider these

proposed amendments and allow amended independent claims 32 and 36 and the dependent claims which variously depend from claims 32 and 36.

New Claims

Applicants have added new independent claim 38 directed to a tablet consisting of a fast dissolve granulation, an active ingredient, mannitol, sucralose, a favor, a disintegrant, corn starch and silicon dioxide wherein the fast dissolve granulation consists essentially of a portion of the mannitol and a low melting point compound that melts or softens at or below 37°C selected from the group consisting of hydrogenated vegetable oil, and partially hydrogenated vegetable oil, and wherein the low melting point compound comprises less than about 20% (wt/wt) of the fast dissolve granulation and from about 0.01% to about 2.5% (wt/wt) of the tablet, and wherein the tablet has a hardness of less than about 1.7 kP. Support for this claim is found in Examples 1,2, and 8 of the specification and paragraphs 28 and 33-35 of the specification, for example.

New dependent claim 39 depends from claim 38 and adds the limitation of a souring agent. Support for this claim may be found, for example, in Example 8 and paragraph 35 of the specification.

Applicants believe that these new claims further point out and distinguish Applicants' invention. Accordingly, Applicants respectfully request that the Examiner enter and allow new claims 38 and 39.

Rejection Under 35 USC §103 – Wehling in view of Mauger

Claims 1, 5 8-10 and 12 stand rejected under 35 USC §103 over Wehling et al. (US 5,178,878) in view of Mauger et al. (US 5,728,403, herein "Mauger"). The rejection is rendered moot as to claims 1, 5 8-10 and 12 which have been cancelled with the current amendment.

Rejection Under 35 USC §103 – Mizumoto in view of Mauger

Claims 1,5, 8-10, 12 and 32-37 stand rejected under 35 USC §103 over Mizumoto et al. (US 5,576,014) in view of Mauger et al. (US 5,728,403, herein "Mauger"). The rejection is rendered moot as to claims 1,5, 8-10 and 12 which have been cancelled with the current amendment.

Mizumoto teaches a composition that achieves the desired dissolution properties by combining low moldability and high moldability saccharides (see col. 5., lines 60-67 and Claim 1). Mizumoto clearly sets forth that the desirable features of the Mizumoto composition are derived from combining at least one of a "high moldability saccharide" and at least one of a "low moldability saccharide" (Col. 5 lines 12-67).

Applicants' independent claims 32 and 36 have been amended herein to add the limitation of a single saccharide. Applicants believe that these amended claims further point out and distinguish Applicants' invention, particularly the fact that only one saccharide is used in Applicants invention.

In contrast to Applicants' invention, Mizumoto neither teaches or suggests that a single saccharide is required (Mizumoto requires at least two saccharides with specified moldabilities). Mizumoto stresses the importance of having both low and high moldability saccharides present and teaches that that they should be granulated together to get the best characteristics of each (col. 5, lines 52-66). Mizumoto teaches in Column 5 lines 18-22 that using one saccharide alone does not yield a tablet of adequate hardness and quick disintegration/ dissolution. Mizumoto explicitly discusses the deficiencies of using one saccharide including experimental support for this position in column 5 lines 23-41. Thus, because Mizumoto teaches that two saccharides are necessary and expounds on the deficiencies of using only one saccharide, Mizumoto teaches away from Applicants' invention as Applicants' tablet which is both fast dissolving and of adequate hardness is formed using only a single saccharide.

Additionally Mizumoto teaches that not only are two saccharides needed to achieve a tablet of adequate hardness with quick dissolve properties, but also that simple physical mixing of the two saccharides will not yield a tablet having the desired physical properties. See Col. 5, lines 42-51. Mizumoto teaches that special processing of the two saccharides is needed to achieve a tablet of adequate hardness with the desired quick disintegration. *Id.*

Mizumoto discusses the special processing of two saccharides with specific properties, but nowhere does Mizumoto either teach or suggest that a saccharide and a low melting point compound may be combined in a granulation; and/or or that a saccharide in combination with a low melting point solid forms a fast dissolving granulation and/or that the fast dissolving granulation comprises about 30% to about 75% of the weight of the fast dissolve tablet as Applicants' claims require. Further, Mizumoto provides no suggestion or motivation to substitute a low moldability saccharide or a high moldability saccharide with a low melting point compound to create a fast dissolving tablet.

The Examiner has indicated that Mizumoto lists lubricants. The listing of lubricants in Mizumoto is a general listing of optional lubricants. Further, of the lubricants listed in Mizumoto in column 13, lines 50-65, magnesium stearate, talc and stearic acid have melting points substantially above 37°C. No distinction is made in Mizumoto as to any merit in using a low melting point compound and/ or there is no teaching or suggestion in Mizumoto of a low melting point compound that melts below 37°C in combination with a saccharide that forms a fast dissolving granulation. Thus, Mizumoto provides no motivation for selecting a low melting point compound.

Mizumoto also does not provide a reasonable expectation of success combining a low melting point compound with a saccharide to form a fast dissolve granulation or any guidance as to the amount of such a granulation that would need to be used in a tablet to form a fast dissolve tablet. Mizumoto focuses on achieving a compression molded formulation showing quick disintegration and fast dissolution by inclusion of granules comprising at least two saccharides – one with low moldability properties and one with high moldability properties and provides no motivation for using a fast dissolve granulation comprising a saccharide and a low melting point compound.

The deficiencies of Mizumoto are not cured by Mauger. Mauger is directed to a taste masking coating that melts in the stomach not to a fast dissolving tablet (see abstract, column 1, lines 56-65 and claim 1). The coating is a mixture of triglycerides and a polymer with the coating intended to remain intact until the tablet reaches the stomach (col. 2 lines 21-29). As the Examiner notes (citing Mauger col. 2, lines 39-63) on page 6 last line of the Office Action, the coating of Mauger “melts”. Melting means undergoing or causing to undergo the transition from solid to liquid [e.g. a phase change], while dissolving is to cause a substance to pass into solution. See Dorlands Medical Dictionary on line at www.mercksource.com. Thus, the attribute of the coating of Mauger is to undergo a physical phase change in the warmth of the stomach as opposed to dissolving in the mouth. Arguably, Mauger doesn’t even teach a fast dissolve coating much less a fast dissolve tablet.

The Examiner has stated in the first paragraph of page 13 of the Office Action that the Examiner relied upon Mauger “to demonstrate the teaching that it is known to incorporate mixtures of mono-, di- and triglycerides, whereby the glycerides provide for taste-masking of drugs and enables a composition to melt at body temperature.” The fact that a material is able to taste mask and melt at body temperature does not teach or suggest a fast dissolving material. In fact, taken as a whole, it suggests a delay in dissolution until the drug has passed the sensory region where taste is detected. As noted above, Mauger explicitly states that the

coating is intended to remain intact until the tablet reaches the stomach (col. 2 lines 21-29). It is well established that a prior art reference must be considered in its entirety, i.e. as a whole, including portions that would lead away from the claimed invention. See MPEP § 2141.02 citing *W.L. Gore & Associates, Inc. v. Garlock, Inc.*, 721 F.2d 1540, 220 USPQ 303 (Fed. Cir. 1983). Mauger does not teach or suggest a fast dissolving tablet. Mauger explicitly teaches a coating that does not melt until it reaches the stomach, and therefore the coating of Mauger does not permit the contents of the tablet to disperse until the tablet reaches the stomach.

Applicants' claims 32 and 38 claim a single saccharide as an element of the fast dissolve granulation. Mauger provides no teaching, suggestion, or motivation to use a saccharide even in the coating disclosed in Mauger much less any other capacity. Further, Mauger provides no teaching disclosure or motivation to use a fast dissolve granulation in a tablet in any capacity coating or otherwise. Accordingly, Mauger does not disclose, suggest or provide motivation for combining saccharide with a low melting point solid form to a fast dissolving granulation, and no teaching, suggestion or motivation for forming a tablet wherein about 30% to about 75% of the weight of the tablet is a fast dissolve granulation of a saccharide and a low melting point solid as Applicants' claims 32 and 38 require.

As claims 33-35 variously depend from claim 32 and claim 37 depends from claim 36, the present amendments to claims 32 and 36 adding the limitations of a single saccharide, the fast dissolve granulation including a portion of the single saccharide and reciting a hardness of less than about 1.7 kP, apply to claims 33-35 and 37. Accordingly, the amendments also further distinguish claims 33-35 and 37 from Mizumoto and/or Mauger for the reasons discussed above.

Thus Mauger neither teaches or suggests the elements needed to cure the identified deficiency of Mizumoto - namely Mauger does not teach or suggest that a saccharide and a low melting point compound may be used to form a fast dissolving tablet composition and/or or that a single saccharide in combination with a low melting point solid forms a fast dissolving granulation and/or that the fast dissolving granulation comprises about 30% to about 75% of the weight of the tablet.

There is no teaching or suggestion in Mizumoto, Mauger or in the combination of Mizumoto and Mauger of Applicants' invention of a combination of a single saccharide and low melting point compound to form a fast dissolving granulation for use in a fast dissolving tablet.

In view of at least these distinctions and the fact that Applicants have amended independent Claims 32 and 36 to add the limitation of a single saccharide, the fast dissolve

granulation including a portion of the single saccharide and reciting a hardness of less than about 1.7 kP, Applicants respectfully request that the Examiner withdraw the rejection of independent claims 32 and 36 and claims 33-35, and 37 which variously depend from claim 33 and 36 under 35 USC §103 over Mizumoto. (US 5,178,878) in view of Mauger et al. (US 5,728,403).

Rejection Under 35 USC §103 – Makino

Claims 1, 5, 8, and 9 stand rejected under 35 USC §103 (a) over Makino (U.S. 5,501,861, herein "Makino"). The rejection is rendered moot as to claims 1, 5, 8, and 9 which have been cancelled with the current amendment.

Rejection Under 35 USC §103 (a) - Shimizu

The Examiner has stated that claims 1 8-9 14, 32 and 34-36 stand rejected under 35 USC §103 over Shimizu et al. (U.S. 6,299,904 B1, herein "Shimizu"). The rejection is rendered moot as to claims 1 and 8-9 which have been cancelled with the current amendment. Applicants' note that claim 14 was cancelled previously and accordingly is not pending.

As the Examiner states, Shimizu teaches a composition comprising a pharmaceutically active ingredient, one or more sugar alcohols selected *from the group consisting of* sorbitol, maltitol, reduced starch saccharide, xylitol, reduced palatinose and erythritol, and a hydroxypropylcellulose.

Nowhere does Shimizu disclose or suggest the combination of a single saccharide and low melting point compound to form a fast dissolving granulation wherein the fast dissolving granulation comprises about 30% to about 75% of the weight of the tablet as independent claims 32 and 36 set forth.

Shimizu teaches a combination of one or more of a limited number of sugar alcohols with the very hydroscopic material hydroxypropylcellulose. Nowhere does Shimizu teach or suggest a fast dissolve granulation of a low melting point compound and a saccharide and/or that such a granulation should comprise about 30% to about 70% of the tablet by weight and/or that the amount of low melting point compound should be about 0.01% to about 2.5% (wt/wt) of the tablet. Accordingly, Shimizu does not set forth or infer every claim element of Applicants' claim 1. Nor does Shimizu provided any suggestion or motivation to prepare a fast dissolve granulation much less a fast dissolve granulation as described and claimed by applicants.

The Examiner has cited Col. 8, lines 5-8 of Shimizu for a tablet of hardness of about 2 to about 20 kg. Applicants have currently amended claims 32 and 36 to recite a tablet of a hardness of less than about 1.7 kP. Applicants' claim is supported, for example, in Example 8 which recite that for compositions 1, 2, of Example 8, the hardness ranges were 0.45 – 1.4 kP, and 0.7 – 1.7 kP respectively. Thus, the hardness range claimed by Applicants is consistent with the hardness measured for exemplary embodiments of Applicants' composition and substantially lower than the range of 2-20 kg of Shimizu cited by the Examiner or the preferred hardness range of Shimizu which is about 4 to about 15 kg. (See Shimizu Col. 8, line 5-9.)

One skilled in the art recognizes that tablet hardness may impact a number of properties of a tablet including for example, processability, robustness and dissolution behavior. As the data presented in Example 8 shows, Applicant's composition is tabletable to form a tablet with substantially lower hardness than that of Shimizu. Namely, in contrast to Shimizu whose tablet hardness is in the range of 2-20 kg and preferably 4-15 kg, Applicants' composition forms a satisfactory tablet with a hardness about 1.7 kP or lower.

As claims 34 and 35 variously depend from claim 32, the present amendment to claim 32 reciting a hardness of about 1.7 kP or lower applies to claims 34-35. Accordingly, the amendment also further distinguishes claims 34-35 from Shimizu for the reasons discussed above.

In view of at least these distinctions and the fact that Applicants have amended independent Claims 32 and 36 to further specify a hardness of less than about 1.7 kP. Applicants respectfully request that the Examiner withdraw the rejection of independent claims 32 and 36 and claims 34 and 35 which depend from claim 32 under 35 USC §103 over Shimizu et al.

Comments Regarding Examiner's Response to Applicants' Arguments in Response of 04/01/08

Applicants thank the Examiner for considering Applicant's Arguments and amendments filed 04/01/08 and withdrawing the rejections of claim 1 under 35 U.S.C. 112 1st paragraph, claims 1-4,5,7-9 and 14 under 35 USC 102 (b) over Mizumoto et al. and Claims 1, 4, 5, 7-9 and 14 under 35 U.S.C. 102(e) over Shimizu.

Applicant's have reviewed and considered the Examiner's response to their amendments and arguments filed 04/01/08. Applicants believe that the current amendments and the detailed comments provided herein above address the issues set forth in the

Examiner's responsive comments regarding the rejection of claims under 35 U.S.C. § 103(a) over Mizumoto in view of Mauger.

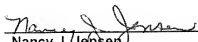
Applicants have cancelled claims herein which were rejected under § 103(a) over Wehling in view of Mauger and under 35 U.S.C. § 103(a) over Makino. Cancellation of these claims should not be viewed as agreement with the Examiner's comments, however the cancellation renders issues related to these claims moot at this time

CONCLUSION

In view of the amended claim set presented herein and the above remarks, Applicants respectfully request that amended claims 32 and 36 and claims 33-35 and 37 which variously depend from claims 32 and 36 be allowed and that new claims 38 and 39 be entered and allowed.

Should the Examiner believe that anything further is desired in order to place the application in even better condition for allowance, the Examiner is invited to contact Applicant's representative at 804-257-2544.

Respectfully submitted,



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